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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,615	07/08/2003	Clemens Hendricus, M. Kocken	2183-6041US	8276

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EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Applicant 09/30/03 RA

Office Action Summary	Application No.	Applicant(s)	
	10/615,615	KOCKEN ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *11-26 and 31-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/08/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of a preliminary amendment, filed 07/08/2003. Claims 1-44 are pending in this application. Pursuant to a restriction requirement discussed below, claims 1-10 and 27-30 are under examination in this action and claims 11-26 and 31-44 are withdrawn from consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office (EPO/ 00204697.7) on 12/22/2000. It is noted, however, that applicant has not filed a certified copy of the EPO application as required by 35 U.S.C. 119(b). Applicant is required to file a certified copy of said application.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted. The groups are as follows (each group designated with a roman numeral):

I. Claims 1-10 and 27-30, drawn to a method of producing mRNA encoding a Plasmodium Apical Membrane Antigen-1 (AMA-1) ectodomain.

II. Claims 11-26, 32 and 33, drawn to nucleic acid molecules encoding a Plasmodium AMA-1 ectodomain.

III. Claims 34-44, drawn to compositions of and methods for diagnosis with, a vaccine comprising a Plasmodium AMA-1 ectodomain.

The inventions listed in Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because under PCR Rule 13.2 which indicates that unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features (i.e. technical features that define a contribution which each of the inventions considered as a whole makes over the prior art). In the instant application, the special technical feature for Group I is AMA-1 ectodomain expression in yeast. However, this special technical feature is not a novel contribution over the art, as AMA-1 has previously been expressed in yeast. (e.g. Kocken et al. Infect. Immun. 1999 January; 67(1):43-49; teaching *Plasmodium vivax* AMA-1 expression in *Pichia pastoris*). In Group II, the special technical feature for a nucleic acid molecule is explicitly the particular nucleic acid structure with the attendant corresponding function. Therefore, a particular nucleic acid sequence or molecule encoding a particular AMA-1 ectodomain would constitute a distinct special technical feature as compared to a distinct sequence. Lastly, the special technical feature in Group III is directed to use of an ectodomain as a vaccine, which is a distinct structure having an attendant specialized function not necessary in the preceding two groups. As such a search for one group would not be co-extensive with a search for another. Furthermore, as was pointed out, the special technical feature for Group I is not a novel contribution over the prior art, thus there is a lack of unity of invention on this ground as well. In sum, restriction is deemed appropriate given the lack of unity of invention.

During a telephone conversation with Applicant' representative, Brett Crocket, on September 13, 2004, a provisional election was made without traverse to prosecute the invention

of Group I, claims 1-10 and 27-30. Applicants must affirm this election in replying to this Office action. Claims 11-26 and 31-44 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

The information disclosure statement (IDS) filed 07/08/2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered, because there is not a copy in the record for each of the references crossed-through in the IDS submitted herewith.

Sequence Listing Rules Compliance

Figure 1 discloses sequences that are not properly identified with sequence identifiers (i.e. "SEQ ID NO:"). Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. In addition, additional sequences are disclosed in the specification on pages 19 and 21. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02. If said sequences were originally submitted in both electronic and paper format, then applicant is only required to make proper amendment to the Brief Description of the Drawings (i.e. with proper sequence identifiers). However, if applicant has not previously submitted said sequences, then a new submission is also required (i.e. CD-ROM/CD-R, Paper Copy and Attorney Declaration).

Specification

The use of the trademark "Prism" and "CODOP" has been noted in this application (Spec. pages 19 and 21). Trademarks should be capitalized and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Objections

Claims 1 and 8 are objected to because of the following informalities: claim 1 recites the acronym "AMA-1" and claim 8 recites "FVO", i.e. Vietnam Oak Knoll, without providing the corresponding definitions respectively. In addition, claim 1 would be grammatically correct if an indefinite article were placed before the term "Plasmodium" to signify that the mRNA is encoding an ectodomain from a Plasmodium (genus of parasites).

Claim 27 is drawn to a non-elected claim (i.e. nucleic acid of claim 11). The claim should be properly amended to incorporate the necessary embodiments, thus removing dependence from a non-elected claim. In the interest of furthering prosecution the claim is examined as though it contains the necessary embodiments. However, appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

1. **Claims 1-10 and 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Base claims 1 and 27 recite the term "and/or" which confers ambiguity as to what the nucleic acid molecule is encoding. The claim is directed to a nucleic acid molecule encoding an ectodomain (A) or functional part (B), derivative (C) and/or analogue thereof (D). First, as written the claim is unclear as to whether D is an analogue of A, B or C. Second, it is unclear whether the nucleic acid is encoding A or B and C and D, thus four different molecules, or A or B and C or D. Furthermore, by reciting both "or" and "and/or" the claims are directed to a convoluted and indiscernible number of possibilities. In sum, because of the claim language there is a great deal of ambiguity and indefiniteness, thus conferring the claims' metes and bounds indeterminable. In addition, the claim recites "functional part" but it is unclear, as written, whether this limitation is directed to the ectodomain; in this regard it would be remedial to include the term "thereof" after the term "functional part".

Claim 2 recites the phrase, "allowing for expression", but it is unclear if this embodiment entails an additional component, element or step necessary for expression, or if this embodiment is simply an extension or intrinsic property of the yeast cell comprising a nucleic acid molecule encoding an AMA-1 ectodomain. For example, if there is an additional step or component, then the claim as written omits an essential element or step necessary for the method of producing said ectodomain.

Claims 3 and 28 recite the term "purifying", which is a subjective and relative term, thus conferring ambiguity and indefiniteness to the claim.

Claim 6 recites the number "20" without any apparent meaning or relationship to any particular embodiment of claim 6 or base claim 1. Therefore, as written the claim is vague and indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-10 and 27-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. More specifically the claims are directed to a genus of nucleic acid molecules that encode an AMA-1 ectodomain or a part, derivative or analogue thereof, with a single disclosed functionality – the requirement that each molecule encodes an antigen that will produce protective immunity. (e.g. Specification, p. 5, ¶ 1; p. 12, ¶ 2; p. 14, ¶ 2; p. 15, ¶ 2; p. 16, ¶ 1). In other words, the invention is directed to a genus in terms of any nucleic acid molecule encoding any portion of any Plasmodium AMA-1 ectodomain having protective immunogenic functionality. The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and

structure or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus.

The specification does not contain a sufficient number of examples of particular embodiments for such nucleic acid molecules. The instant specification provides limited guidance for one of skill to envisage the vast number of embodiments claimed. For example, five different structures (i.e. amino acid residues 25-442, 303-442, 303-544, 419-544 and 97-545 of the sequence provided in Fig. 1) from a single species of Plasmodium (*falciparum*) are show to react with a monoclonal antibody. (Spec. pp. 24-26). Of the five only three are show to reactive with the parasite-inhibitory antibody. (e.g. p. 24, bottom ¶). There is no further information provided to clarify the different regions or sequences (i.e. fragments, analogues or derivatives) that actually inhere the immunogenic functionality. Of course, even if such clarification were provided, it would be limited to a single species of Plasmodium, if not a single strain. (See infra, Fandeur et al. Am. J. Trop. Med. 1998; 58(2):225-31). Moreover, significance of any further clarification could be host-specific. (Id.). The disclosure provides and additional two fragments (i.e. amino acid residues 97-442 and 97-318), which are shown to have some *in vitro* inhibitory activity (i.e. antibodies to said fragments result in 50-60% inhibition of invasion). However, even a single amino acid change in any of the disclosed structures could result in a distinct functionality in regard to the antigen eliciting protective immunity *in vivo*, notwithstanding *in vitro* results disclosed. In sum, the disclosure is not descriptive of the complete structure of a representative number of species, which the claims encompass, as one of ordinary skill in the art cannot envision all Plasmodium AMA-1 ectodomains, functional fragments, derivatives or analogues thereof, based on the teachings in the specification.

One of skill in the art would appreciate the fact that particular Plasmodium AMA-1 ectodomains, fragments, derivatives or analogues, are not necessarily interchangeable, because there can be Plasmodium variant-, strain-specific or even host specific immunity. (e.g. Fandeur et al. Am. J. Trop. Med. 1998; 58(2):225-31; e.g. Abstract; indicating Variant- and Strain-specific immunity in a simian species infected with *Plasmodium Falciparum*). There it logically follows, as amongst the broad number of embodiments of Plasmodium AMA-1 ectodomains claimed, there would not necessarily be any functional interchangeability.

Given the enormous breadth of the nucleic acid structures encompassed by the rejected claims, and given the limited description from the instant specification of such structures, the skilled artisan would not have been able to envision a sufficient number of specific embodiments to described the broadly claimed genus of nucleic acid molecules encoding a Plasmodium AMA-1 ectodomain, functional fragment, derivative or analogue. Moreover, an applicant claiming a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from other species. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1-3, 5-6, 9-10 and 27-30 are rejected under 35 U.S.C. 102(a) as being anticipated by Kocken et al. (Infect. Immun. 1999 Janurary; 67(1):43-49; see whole document).

The claims are directed to expression of any Plasmodium apical membrane antigen 1 (AMA-1) in yeast, such as *Pichia pastoris*. More particular claims are directed the nucleic acid encoding said ectodomain to have at least one site removed where the site could otherwise be glycosylated. The limitation, "modification" is interpreted as broadly as reasonable to read on any change/alteration of the site (e.g. enzymatic or structural). In addition, that the AMA-1 protein expressed is approximately 83 kDa in size is interpreted, as broadly as reasonable, thus any AMA-1 protein would read on this limitation.

Kocken et al. teach expression of *P. vivax* AMA-1 in *P. pastoris* to elicit protective immunity in *Macaca mulatta* monkeys. (e.g. Abstract). More particularly, particular sites that are normally glycosylated are mutagenized so as to preclude subsequent glycosylation. (e.g. p. 44, col. 1, ¶ 3). In addition, the proteins expressed are purified through such steps as dialysis, precipitation or ion exchange chromatography. (e.g. p. 44, last ¶, bridging to col. 2). In sum, Kocken et al. anticipates the rejected claims.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The

filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

4. Claims 1-10 and 27-30 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-10 and 27-30 of copending Application No. 10/468,761.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims are word for word the same in each application, thus are directed to the same invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

GERRY LEFFERS
PRIMARY EXAMINER